

EDITORIAL

Follow-Up of Melanoma Patients: The Need for Evidence-Based Protocols

Anne Brecht Francken, MD, PhD and Harald J. Hoekstra, MD, PhD

Department of Surgical Oncology, Groningen University Medical Center, Groningen, The Netherlands

Over the past decade it has become clear that sensible, safe, evidence-based guidelines are required for the follow-up of cancer patients. Patient expectations for high-quality care have increased, although ever-increasing restrictions are being imposed on expensive health care resources. Therefore the need for constructive, cost-effective, high-quality guidelines for patients with a range of cancer types has now become urgent.

For patients who have had a melanoma frequent clinical consultation and regular imaging studies are still common practice in many centres, despite a lack of evidence regarding their influence on overall survival, disease-free survival or quality of life.^{1,2} Why is this so? In the first place we cling to historical precedent. It is well known that this form of cancer is unpredictable, and the assumption has therefore been made that it should be monitored frequently and carefully. Secondly, it seems appropriate to detect recurrence at an early stage, since effective treatment of local, in-transit and regional node metastases offers the possibility of cure, and long-term survival can also follow complete resection of systemic metastases. Third, patient satisfaction and patient reassurance are provided by frequent clinical consultation.

In this and a recent issue of *Annals of Surgical Oncology* two interesting studies are reported.^{3,4} The study of Meyer et al. is a retrospective report of 118 American Joint Committee on Cancer (AJCC) stage II and III melanoma patients who underwent regular structural imaging with a minimum follow-up of 2 years. Recurrence occurred in 35% ($n = 43$), of which 43% ($n = 15$) were distant metastases. However, only 7% ($n = 3$) of these patients

were asymptomatic and had their recurrence detected by routine imaging. Another 26% ($n = 11$) were detected by routine clinical follow-up, including medical history and physical examination.^{1,5,6} This study is consistent with previous reports that found two-thirds of melanoma recurrences were patient detected.

The study of Morton et al. evaluated 108 patients with AJCC stage IIIA and IIIB melanoma who were prospectively enrolled in a monitoring schedule of 6-monthly chest X-rays (CXR) in addition to clinical follow-up. They found metastases in 21% ($n = 23$) of the patients, which were detected in 48% ($n = 11$) by surveillance CXR. The other pulmonary metastases were not detected by CXR surveillance. The authors found sensitivity and specificity for surveillance CXR was 48% [95% confidence interval (CI) 0.27–0.68] and 78% (95%CI 0.77–0.79), respectively. In only 13% ($n = 3$) was metastasectomy considered appropriate. Moreover, 19 patients had a false-positive result for melanoma metastasis, 10 of whom underwent a pulmonary biopsy. This study confirms earlier results of retrospective studies: routine CXR does not seem to contribute to an improvement in survival of melanoma patients, nor is it cost effective.^{7–9}

The results of these two valuable studies underscore the limited value of routine imaging in the follow-up of melanoma patients. However, both studies have their shortcomings. First the retrospective nature by the study of Meyer et al. and the lack of a control group in the study by Morton et al. reduce the level of evidence according to standard methodology. Second, the low number of patients in both studies makes them underpowered due to the low rate of events. Nevertheless, this type of clinical report is of great importance since large-scale prospective studies and appropriately designed randomised studies are extremely difficult to perform in this particular field; they might even be a waste of time and money based on current knowledge.

On the other hand, it is important to recognise that evidence documenting the value of clinical follow-up in melanoma patients is still inadequate and that prospective studies are required to determine which format will offer best care not only in terms of survival but also in quality of life. Most patients prefer frequent follow-up consultations and imaging studies to detect early recurrent disease. However, frequent visits and imaging studies such as conventional X-rays, spiral computed tomography (CT) scans and positron emission tomography (PET) scans do not seem to alter their outcome. Therefore, it might be more worthwhile to focus on different aspects of follow-up. It becomes increasingly obvious that follow-up schedules should be much more patient tailored. Several current national guidelines for melanoma management fail to clearly differentiate between patients with various AJCC/International Union against Cancer (UICC) stages of melanoma disease when recommending follow-up protocols, although it has been shown that the risk of recurrence ranges widely according to disease stage.^{10,11} In relation to this, the current opportunity for accurate nodal staging afforded by sentinel node biopsy is extremely valuable, regardless of its potential survival benefit. The excellent prognosis of patients who are sentinel node negative means that intensive follow-up is probably not required, while those found to be sentinel node positive have a much greater risk of recurrence and may therefore warrant more intensive follow-up. A further point to be considered is that, to improve patient satisfaction regarding follow-up, new guidelines should take into account patient characteristics such as age, accessibility to health care and level of anxiety. The melanoma specialist should have the opportunity to have flexibility in the interpretation of new guidelines, so that a follow-up schedule can be recommended to fit the individual patient. Finally, education of patients is likely to be the most important aspect of follow-up and should be completely integrated in the follow-up program. Several recent studies have shown that the detection of recurrence is most commonly by patients and their partners, rather than by doctors at routine follow-up visits.^{5,7,12–14} The current melanoma follow-up study (MELFO), being undertaken in The Netherlands seeks to determine whether improved patient education and reduced follow-up is a safe and cost-effective approach to melanoma follow-up.¹⁴

permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

REFERENCES

1. Francken AB, Bastiaannet E, Hoekstra HJ. Follow-up in patients with localised primary cutaneous melanoma. *Lancet Oncol*. 2005;6:608–21.
2. Nieweg OE, Kroon BB. The conundrum of follow-up: should it be abandoned? *Surg Oncol Clin N Am* 2006;15:319–30.
3. Meyers MO, Yeh JJ, Frank J, Long P, Deal AM, Amos KD, et al. Method of detection of initial recurrence of stage II/III cutaneous melanoma: analysis of utility of follow-up staging. *Ann Surg Oncol*. 2008. doi:10.1245/s10434-008-0238-y
4. Morton RL, Craig JC, Thompson JF. The role of surveillance chest x-rays in the follow-up of high-risk melanoma patients. *Ann Surg Oncol*. 2008. doi:10.1245/s10434-008-0207-5
5. Francken AB, Shaw HM, Accortt NA, Soong SJ, Hoekstra HJ, Thompson JF. Detection of first relapse in cutaneous melanoma patients: implications for the formulation of evidence-based follow-up guidelines. *Ann Surg Oncol*. 2007;14:1924–33.
6. Francken AB, Thompson JF, Bastiaannet E, Hoekstra HJ. [Detection of the first recurrence in patients with melanoma: three quarters by the patient, one quarter during outpatient follow-up]. *Ned Tijdschr Geneesk*. 2008;152:557–62.
7. Hofmann U, Szedlak M, Rittgen W, Jung EG, Schadendorf D. Primary staging and follow-up in melanoma patients—mono-center evaluation of methods, costs and patient survival. *Br J Cancer*. 2002;87:151–7.
8. Tsao H, Feldman M, Fullerton JE, Sober AJ, Rosenthal D, Goggins W. Early detection of asymptomatic pulmonary melanoma metastases by routine chest radiographs is not associated with improved survival. *Arch Dermatol*. 2004;140:67–70.
9. Mooney MM, Mettlin C, Michalek AM, Petrelli NJ, Kraybill WG. Life-long screening of patients with intermediate-thickness cutaneous melanoma for asymptomatic pulmonary recurrences: a cost-effectiveness analysis. *Cancer*. 1997;80:1052–64.
10. Francken AB, Accortt NA, Shaw HM, Colman MH, Wiener M, Soong SJ, et al. Follow-up schedules after treatment for malignant melanoma. *Br J Surg*. 2008;95:1401–7.
11. Balch CM, Soong SJ, Gershenwald JE, Thompson JF, Reintgen DS, Cascinelli N, et al. Prognostic factors analysis of 17,600 melanoma patients: validation of the American Joint Committee on Cancer melanoma staging system. *J Clin Oncol*. 2001;19:3622–34.
12. Weiss M, Loprinzi CL, Creagan ET, Dalton RJ, Novotny P, O'Fallon JR. Utility of follow-up tests for detecting recurrent disease in patients with malignant melanomas. *JAMA*. 1995;274:1703–5.
13. Baughan CA, Hall VL, Leppard BJ, Perkins PJ. Follow-up in stage I cutaneous malignant melanoma: an audit. *Clin Oncol (R Coll Radiol)* 1993;5:174–80.
14. Francken AB, Bastiaannet E, Hoekstra-Weebers JEHM, Schaapveld M, Hoekstra HJ. MELFO: prospective randomized trial for the evaluation of a theoretical follow-up schedule in cutaneous melanoma patients; 2006. <http://www.ikcnet.nl/trials>. Accessed 18 November 2008.

OPEN ACCESS This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which